

# Value of Radio-iodine Therapy in the Management of Basedow's Disease Experience of the Nuclear Medicine Department – Chu Hassan II Fes

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## Abstract

Used for the first time in 1941 in the United States by Hertz and Roberts for the treatment of hyperthyroidism in Grave's Disease, radioactive therapy (RAI) has been able to gain its place within the already existing therapeutic arsenal by being efficient, easy to use and minimally invasive. Our work is a retrospective study of 71 patients collected at the Department of nuclear medicine of the University Hospital Hassan II of Fez, over a period of 6 years from 2013 to 2019. The purpose of this study is to determine the place of radioiodine therapy in the treatment of Graves' disease in our context and to evaluate its results.

**Keywords:** Grave's disease • Radioiodine therapy • Basedow disease • Thyroid

## Introduction

Graves' disease is an autoimmune disorder of the thyroid gland that manifests as hyperthyroidism, a homogeneous goitre and sometimes exophthalmos. Its treatment consists of the administration of SADs for 12-24 months. When this treatment was discontinued and due to the high number of relapses among treated patients, Iodine-131 irradiation became the treatment of the first choice. This work aims to demonstrate the interest of radio-iodine in the treatment of Basedow's disease through a study of 71 cases.

## Patients and Methods

This is a retrospective study of 71 cases of Basedow disease admitted between 2013 and 2019 for RAI at the Department of Nuclear Medicine of the CHU HASSAN II of Fez.

The diagnosis of Basedow disease consisted of an analysis of clinical (palpitations, weight loss, exophthalmos) and biological (T4 and TSH, TRAKS positive) data. Confirmation by thyroid scintigraphy: intense and homogeneous capture of regular contour without palpable nodule.

All our patients received a course of irradiation with iodine-131, the dose being between 8 and 15 mCi with a median of 12 mCi; after a 5-day interruption of SADs.

Clinical and biological monitoring was performed for 6 weeks, 3, 6 and 12 months.

## Results

The average age of the patients was 45 years with a clear female predominance, sex ratio F/H=7.8. Treatment with iodine-131 was indicated as the first line in one case (1.4%), as the second line in 69 cases (97.18%) and after subtotal thyroidectomy in one case (1.4%). The second cure of irradiation was indicated in 7 patients and the third cure in one patient after an average duration of 6 months due to the persistence of hyperthyroidism after the first

course. The results of the biological control for 6 weeks, 3 and 6 months after RAI showed euthyroidism in 14 patients (20%), hypothyroidism in 46 patients (65%) and hyperthyroidism in 11 patients (15%). On the other hand, the biological control found, 12 months after RAI, euthyroidism in 16 patients (i.e. 22%), hypothyroidism in 50 patients (71%) and hyperthyroidism in 5 patients (7%). No acute complications were observed.

## Discussion

### Age

The peak incidence of Graves' disease is between 30 and 60 years of age, although it can occur at any age [1]. In our study, we found an average age of 45 years with extremes of 17 and 75 years. Studies from Morocco [2-4], Tunisia [5,6], China [7] and the United States [8] have reported mean ages of around 43 years. A similar study in Senegal [9], however, showed a slightly lower average age of 34.6 years.

### Sex

The predominance of women in Graves' disease is well established. This is consistent with our results where 88.7% of patients are women compared to 11.3% of men; a sex ratio of 7.8. This female predominance has also been found in both European and African studies.

**Place of iodine-131 irradiation in the treatment of Graves' disease:** Iradotherapy is increasingly used as the treatment of choice for most patients with Graves' disease. It is both effective and safe as a first- or second-line treatment when thyrotoxicosis cannot be controlled by synthetic antithyroid drugs (STDs) [10,11]. However, in the absence of a standardised consensus, there is a wide divergence in treatment trends among practitioners around the world. In a 2011 survey of clinicians, 69% of American Thyroid Association (ATA) members suggested the use of radioiodine removal for a patient with Graves' disease, while only 22% of European, 22% of Chinese, 11% of Japanese and 11% of Korean respondents chose this treatment option. In contrast, the majority of clinicians have opted for RAI therapy in cases of persistent or recurrent hyperthyroidism [12-14].

**1<sup>st</sup> intention:** In our study, RAI therapy was used as first-line treatment in one case (1.4%). First-line irradiation is indeed a routine indication in the United States in 50% to 75% of cases, except for young subjects where it represents only 30% of the options compared to 22% to 50% in Europe [15-18]. However, in another study by Dejax et al. [19] on the treatment of hyperthyroidism in the over 65s with 131I, 21 cases of Graves' disease were treated with 131I, of which four (19%) received iodine as first-line therapy. In the study by Alaya et al. [20], irradiation was used as first-line treatment in 7.5% of patients.

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Almost the same percentage was found in the series of Feleh et al. [6] who used RAI therapy in 7.1% of patients as first-line therapy due to leuko-neutropenia.

**2<sup>nd</sup> intention:** The frequent relapse of the disease, as well as resistance to treatment, leads the clinician to opt for radical treatment. In our series, 131I was indicated as second-line treatment in 97.18% of patients.

Indeed, pre-treatment with SADs before administration of iodine-131 is not mandatory, with some exceptions. Because of the risk of transient worsening of thyrotoxicosis after RAI therapy, older patients, or those with comorbidities such as coronary artery disease, may benefit from pre-treatment [21]. In patients requiring pre-treatment, SADs should be stopped one week before irradiation to allow for a good response. Adjunctive therapy with TSA before RAI may decrease its efficacy (as reported in a meta-analysis [22] from 2007); however, this is not clinically significant with moderate activity. In our study, TSAs were prescribed in 69 cases and discontinued on average 5 days before RAI therapy.

**131I Activity Administered:** Iodine-131 irradiation has been used since 1941, but few well-designed prospective trials are leaving many questions about indications, optimal dose, efficacy and side effects [23]. Furthermore, there is no consensus on the optimal activity to administer. The objectives differ from one team to another. A therapeutic choice must therefore be made between standard activities set empirically, with early onset of hypothyroidism, and lower calculated activities, aimed at preserving normal thyroid function with later onset of hypothyroidism. However, in the latter case, the rate of therapeutic failure is higher, leading to the need for a second or even third course of RAI therapy [24]. A randomised trial has suggested the superiority of calculated dosing regimens [25] that take into account estimated thyroid weight in grams, desired dose (100 to 200 $\mu$ Ci per gram) and 24-hour radioiodine intake. In addition, another study [26] reported that the use of three fixed-dose amounts, based on the size of the gland as determined by palpation (5, 10 or 15 mCi [185, 370 or 555 MBq]), was also effective. The American Thyroid Association (ATA) and the American Association of Clinical Endocrinologists (AACE) recommend a single activity of 10-15 mCi for optimal treatment of Graves' disease by making the patient hypothyroid [27,28]. In our series, the activities administered ranged from 8 to 15 mCi, with an average of 12 mCi.

## Results of RAI Therapy Treatment

### In the short term

Radioactive iodine treatment is generally well-tolerated in Basedow disease. However, side effects may occur in the days or months following the administration of the drug. In our series, the treatment was very well tolerated in all patients. However, neck pain, swelling and sialadenitis may occur. Graves' disease is associated with increased morbidity and mortality [29,30]. Its treatment decreases mortality [31], while ARF itself does not increase mortality [23]. The relationship between the treatment of hyperthyroidism due to Graves' disease and the course of associated Graves' ophthalmopathy is controversial [32]. Several studies have indeed demonstrated the aggravating effect of RAI on this orbitopathy [33,34]. Approximately 15% of patients may develop ophthalmopathy or aggravation of pre-existing ophthalmopathy after treatment with iodine-131 [35, 36]. Its occurrence has been reported by several authors [37-41] following the use of higher doses of radioiodine than those used in the treatment of Graves' disease. Prophylactic treatment with oral prednisone during and after treatment with iodine-131 may significantly reduce the risk of development or aggravation of ophthalmopathy [36,42]. In the study conducted by Dejax et al. [19], 6 cases of cervical inflammatory reactions were found out of 270 patients treated with RAI therapy. Furthermore, the study conducted by Lyazidi, of all 19 patients in the series, reported that only three patients showed side effects such as headache and anxiety within eight days of taking the drug. Only one patient reported a rebound of hyperthyroid symptoms 15 days after RAI therapy. In contrast, no cervical or systemic inflammatory reactions were noted in all treated patients.

### In the medium and long term:

RAI therapy aims to make the patient hypothyroid. Thus, most patients develop hypothyroidism 2 to 3 months after an administration of 12 to 15 mCi (444-555 MBq). Euthyroidism is achieved within 3-12 months in 50-90% of patients [23]. The incidence of hypothyroidism is 5-50% after the first year and is associated with the dose of RAI therapy. This is followed by an annual hypothyroidism rate of 3-5% that is largely independent of RAI therapy dose [43]. Even with low-dose irradiation therapy, which increases the risk of persistent/recurrent disease, hypothyroidism is inevitable [44]. The study in our series showed that 21% of the patients went to euthyroidism and 68% to hypothyroidism. The "cure" rate was therefore 89%. Persistence or recurrence of hyperthyroidism was noted in 10% of cases.

## Conclusion

Our results and those of previous work on RAI therapy show that the effectiveness of radioactive iodine in the treatment of Graves' disease is well established. Taking into account our socio-economic context, RAI therapy should be a treatment of choice, given its good quality/price ratio and excellent tolerance of treated patients.

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